MEDICAL PROCEEDINGS

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REDAKSIONEEL · EDITORIAL

REKLAME

Die mediese professie het homself 'n baie streng etiese kode opgelê om die gedrag van sy lede te reël, onder meer ook wat betref die publikasie van hul menings in koerante en tydskrifte wat vir leke bedoel is. Hierdie besondere kenmerk van etiese gedrag word formeel uiteengesit in 'n reël wat deur die Geneeskundige Raad gepubliseer is en soos volg lui:

Toelaat dat sy mening oor onderwerpe van geneeskundige of tandheelkundige aard onder sy naam in die lekepers verskyn; met dien verstande dat hierdie reël egter nie van toepassing is in die geval van voltydse publieke geneeskundige of tandheelkundige amptenare wat optree in hul amptelike hoedanigheid nie; of in die geval van amptenare van 'n geneeskundige of tandheelkundige vereniging of genootskap wat ooreenkomstig opdragte van so 'n vereniging of genootskap in hul amptelike hoedanigheid optree nie; of in die geval van praktisyns wat nie 'n privaat praktyk het nie; of in geval van enige mededeling wat alleenlik handel oor vraagstukke van suiwer akademiese aard, openbare gesondheid, hospitaal-administrasie, medies-politieke sake, tandheelkundige en dergelike aangeleenthede, waarin die nodige samewerking van die publiek gesoek word ten einde die beginsels wat alreeds algemeen deur die professie aanvaar is, prakties uit te voer.

Opmerking.—'n Praktisyn wat toelaat dat sy menings oor geneeskundige en tandheelkundige onderwerpe in die lekepers verskyn, sal persoonlik daarvoor aanspreeklik gehou word dat sodanige bekendmaking in die pers nie die vorm van advertensie aanneem nie.

In sy huidige vorm maak die reël 'n besliste onderskeid tussen dokters wat nie privaat praktiseer nie, en dokters wat wel privaat praktiseer. Kollegas wat voltydse kliniese ampte aan 'n universiteit of 'n openbare hospitaal beklee,

ADVERTISING

The medical profession imposes upon itself a very strict ethical code which determines the conduct of its members, *inter alia,* in relation to the publication of their views through lay media. This feature of ethical conduct has been stated formally in a Rule published by the Medical Council, reading as follows:

'Permitting the appearance in the lay press of his opinion on medical or dental subjects with his name appended thereto; provided that this rule shall not apply to whole-time public medical or dental officials acting in their official capacities; or to officers of a medical or dental association or society acting in an official capacity on the instructions of such association or society; or to practitioners not in private practice; or to any communication dealing solely with questions purely of academic interest, public health, hospital administration, medico-political matters, dentistry and the like, wherein the co-operation of the public is necessarily sought in order to give practical effect to principles already generally accepted by the profession.

Note. A practitioner permitting the appearance in the lay press of his views on medical and dental subjects will be held personally responsible that such publication does not constitute advertising.'

The present form of the Rule treats practitioners not in private practice on a distinctly different footing from practitioners in private practice, e.g. colleagues holding full-time clinical appointments on a university or a public hospital establishment are exempt from the restrictions placed upon the publication through lay media of their opinions on medical subjects.

It is recognized that one of the purposes of the Rule is to prevent doctors from advertising themselves in such a way as to attract patients

is byvoorbeeld vrygestel van die beperkinge op die publikasie in die lekepers van hul menings oor mediese onderwerpe.

Daar word erken dat een van die oogmerke van die Reël is om dokters te verhinder om op so 'n manier reklame vir hulself te maak dat hulle pasiënte aanlok, maar dit is ewe onwenslik vir dokters om hulself of hul inrigtings op so 'n manier te adverteer dat hulle pasiënte na een inrigting liewer as na 'n ander, of na 'n besondere inrigting liewer as na 'n private praktisyn lok. Die saak gaan veel verder as selfs dit. Op suiwere navorsingsgebied kan agtereenvolgende en herhaaldelike reklame (hoe dit ook al ontstaan) die indruk wek dat 'n besondere navorsingswerker op 'n besondere navorsingsgebied uitblink, terwyl sy navorsingskollegas wat publisiteit in die lekepers vermy, bes moontlik deur hul gelykes as eminenter en meer gedistingeerd beskou word as diegene wie se name gereeld deur koerantbiljette en koerantopskrifte uitgebasuin word. Die navorsingswerker wat die pers in sulke omstandighede nie verhinder om hierdie soort publisiteit aan hom te verleen nie, ontneem sy navorsingskollegas 'n deel van hul reputasie op 'n manier wat beslis onwaardig en, volgens ons mening, ook onbehoorlik is.

Inderdaad, deur geneeshere wat nie privaat praktiseer nie van die bepalings van die reël vry te stel word 'n dubbele standaard van etiese gedrag geskep. Vir sover dit reklame betref, is dit onwenslik dat die standaard van etiese gedrag wat geverg word van die dokter wat privaat praktiseer anders moet wees as die standaard wat vereis word van praktisyns wat nie privaat praktiseer nie. Indien enigiets eties onbehoorlik is, bly dit onbehoorlik of dit nou al gedoen word deur 'n praktisyn in voltydse of 'n praktisyn in die private praktyk. Dubbele standaarde kan alleen moontlikhede vir misbruike skep.

Die voor die hand liggende onwenslikheid van dubbele standaarde van etiese gedrag vir geregistreerde mediese praktisyns maak dit 'n saak van die allergrootste belang dat die Suid-Afrikaanse Geneeskundige Raad aandag moet bestee aan die anomale posisie wat op die oomblik bestaan. Dit het lank reeds nodig geword om die huidige Reël in verband met reklame, en, in besonder Reël 1 (6), te wysig. Geen praktisyn behoort toegelaat te word om sy menings oor mediese (kliniese) onderwerpe onder sy naam in die lekepers te laat verskyn nie, met uitsondering van voltydse openbare mediese amptenare wat in hul amptelike hoedanigheid optree, of amptenare van 'n mediese vereniging wat in opdrag van sodanige vereniging in hul amptelike hoedanigheid optree.

Logika sowel as billikheid vereis dat alle geregistreerde mediese praktisyns dieselfde etiese verpligtinge opgelê moet word vir sover dit hul kliniese of

to them; but it is equally undesirable for doctors to advertise themselves or their institutions in such a way as to attract patients to one institution rather than another or to a particular institution rather than to a private practitioner. The matter goes even further than this. In the purely research field successive and repeated advertisements (however instigated) may create the impression that a particular medical research worker is pre-eminent in a particular field of research, whereas his research colleagues, who disdain the publicity afforded by lay media, may well be recognized by their peers as far more eminent and distinguished than those whose names have regularly been blazoned across newspaper posters and newspaper headlines. In such circumstances, the research worker who fails to restrain the press from giving him such publicity takes away from other colleagues in the research field something of their reputation in a manner which is distinctly undignified and, we submit, improper.

In effect, the exclusion of practitioners not in private practice from the operation of the Rule creates a dual standard of ethical conduct. It is undesirable that a different standard of ethical conduct should be required from practitioners in private practice as compared with practitioners not in private practice. If an act is ethically improper, it remains improper whether it is performed by a practitioner in full-time or in private practice. Double standards can only open up possibilities of abuse.

The patent undesirability of dual standards of ethical conduct for registered medical practitioners makes it a matter of importance that the South African Medical Council should direct its attention to the currently anomalous situation. There is overdue need to amend the existing Rule relating to advertising, in particular Rule 1 (6). No practitioner should be permitted to allow his opinion on medical (clinical) subjects to be published in lay media under his name, with the exception of wholetime public medical officials acting in their official capacities or officers of a medical society acting in an official capacity on the instructions of such a society.

Logic as well as equity requires that all registered medical practitioners should be placed under the same ethical obligations in respect of their clinical or laboratory duties. This does not, of course, touch upon the right of a medical practitioner to exercise all such public functions as he is entitled to exercise in the same manner as any other citizen, whether this be in the form of standing for political office, serving on public bodies or par-

laboratoriumpligte betref. Dit raak natuurlik nie die reg van 'n mediese praktisyn om enige openbare amp na te streef wat hy, net soos enige ander landsburger, geregtig is om na te streef nie, hetsy deur hom vir 'n politieke betrekking verkiesbaar te stel, in 'n openbare liggaam te dien, aan 'n letterkundige wedstryd deel te neem, of so iets. Daar kan geen beswaar wees teen die gebruik van 'n praktisyn se naam as hy welslae in sulke openbare (nie-mediese) aktiwiteitsfere behaal nie.

Ons erken dat daar sommiges kan wees wat die mening toegedaan is dat ons huidige beperkinge buitensporig eng is, en nie aan die vereistes van ons tyd voldoen nie. Dit is miskien so, en dit is moontlik dat die Geneeskundige Raad te veel beperkinge op die gedrag van geregistreerde praktisyns plaas. Die voorstanders van hierdie sienswyse sal egter erken dat dit 'n ander en heeltemal afsonderlike vraagstuk is. Solank daar etiese beperkinge is op gedrag wat as onbehoorlike reklame bestempel kan word, behoort hierdie beperkinge eenvormig en billik toegepas te word op alle soorte mediese praktisyns, met uitsondering van die genoemde klasse.

ticipating in literary competitions, etc. There can be no objection to a practitioner's name being used in connexion with his successful achievement in such public (non-medical) fields of activity.

We recognize that there may well be a view which regards our existing restrictions as excessively severe and not in keeping with the requirements of the day. This may indeed be so and the Medical Council may have erred on the side of an excess of restraint upon the conduct of registered practitioners. The proponents of this view, however, must recognize that this is a separate and different issue. While there are ethical restrictions upon conduct which may be construed as improper advertisement, these restrictions should operate uniformly and equitably on all classes of practitioners with the exceptions mentioned.

ABSTRACTS

HOSPITAL CONTROL OF STAPHYLOCOCCI

Comments are presented on a discussion by Dr. Ian Maclean Smith and Dr. Mary Godfrey of Iowa on hospital control of staphylococci. Dr. Smith's recommendations were:

(1) Isolate pus-dripping patients.
(2) Enforce rules requiring hand-washings and the wearing of masks.
(3) All personnel should behave as if they might be nasal carriers of staphylococci.
(4) Furlough personnel having boils or carbuncles.
(5) Re-examine and tighten up housekeeping procedures.
(6) Seek epidemiologic consultation from the Department of Health.

[August 1958: J. Iowa M. Soc., **48,** 469.]

BRAIN CHANGES AFTER DRUGS

In the various brain parts of chlorpromazine-penetrated rabbits the administration of 5-HTP caused increases of serotonin concentration which were of greater magnitude and longer duration than those found in animals treated with only 5-HTP. When animals were pretreated with chlorpromazine, the injection of 5-HTP did not produce behavioral hyperexcitation and the animals did not arouse from chlorpromazine tranquilization.

[Costa, E. *et al.* (July 1958): *Biochemical and Electroencephalographic Changes in the Brain of Rabbits Injected with 5-hydroxytryptophan (Influence of Chlorpromazine Premedication)*, Amer. J. Physiol., **194,** 214.]

ECG AND HYPERVENTILATION SYNDROME

The hyperventilation syndrome represents a clinical picture of autonomic nervous and central nervous origin. Psychoneurosis or organic disease of the C.N.S. are possible aetiological factors; it is, however, quite conceivable that organic heart disease may also be present at the same time. The patient's symptoms are probably due to spasm of the intercostal, pectoral or diaphragmatic muscles during the alkalosis induced by hyperventilation.

These symptoms can be reproduced by voluntary hyperventilation or by the injection of adrenaline, but only in patients and not in normal test subjects. Some 15 seconds after the onset of hyperventilation E.C.G. changes occur which disappear again one minute after resumption of normal breathing. Inversion of the T wave is seen, and also, though more seldom, depression of the ST segment. CO_2 tension, pH, and potassium level of the arterial blood are greatly altered. The intravenous administration of 5 mg. Regitine frequently makes it possible to prevent the E.C.G. changes that follow hyperventilation or the injection of adrenaline. An intravenous injection of potassium chloride can suppress in whole or in part the E.C.G. changes induced by hyperventilation. The E.C.G. changes associated with the hyperventilation syndrome are probably to be attributed both to alkalosis and to the stimulation of the sympathetic nervous system caused by the secretion of adrenaline.

[Yu, P. N., Yim, B. J. B. and Stanfield, C. A. (1959): A.M.A. Arch. Int. Med., **103,** 902].

COTTONSEED OIL AND CHOLESTEROL

Upjohn's Lipomul-IV, an emulsion of cottonseed oil, caused a shift in protein distribution in the plasma and some lowering of serum cholesterol.

[Everett, M. A. *et al.* (June 1958): *The Effect of Intravenous Fat on Serum Lipids*, J. Invest. Dermat., **30,** 333.]

LEUKAEMOID REACTIONS IN CARCINOMA

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The first recorded case by Kast[1] in 1903 described a case of carcinoma of the penis of 18 months' duration in which the white cell count was 120,000 per c.mm.; 1% of the cells were myelocytes. Metastatic bone secondaries were present.

Kurpjuweit[2] (also in 1903) reported a case of primary carcinoma of the stomach with bone metastases in which the white cell count was 9,100 per c.mm.; with 11% myelocytes and 6.6% metamyelocytes.

Shoemaker[3] in 1910 described a case of primary carcinoma of the stomach in which the white cell count was 125,000 per c.mm. No details were given.

CASE REPORTS

Case 1. A 28-year-old White male presented with the following history.

Two months before admission he had experienced a sudden onset of pain in the left hypochondrium. A diagnosis of fibrositis had been made by his practitioner, but a few days later the patient noticed a fullness in the left hypochondrium, which later developed into a distinct swelling. A diagnosis of splenomegaly was then made.

On admission the patient complained of a visible swelling in the left hypochondrium. He was also troubled by anorexia and had lost 14 lb. in weight in the past 2 months.

Clinically he was a healthy looking young male showing no evidence of anaemia or jaundice. He had, however, a distended abdomen which, on palpation, revealed a mildly tender spleen extending almost down to the umbilicus. The liver edge was palpable half an inch below the costal margin at the mid-clavicular line.

Investigations revealed a haemoglobin of 13.2 g. %, a haematocrit of 40%, a leucocyte count of 55,100 per c.mm., with 65% neutrophils, 3% monocytes, 12% lymphocytes, 2% eosinophils, 1% basophils, 3% neutrophil myelocytes, 2% neutrophil metamyelocytes and 12% staff cells. The red cells and platelets were normal in number and appearance.

A stained film for alkaline phosphatase of the white cells showed no deficiency in alkaline phosphatase.

Lactic dehydrogenase was 880 units (range 100-270 units). Both serum glutamic oxalacetic and pyruvic transaminases were normal throughout the illness.

A bone marrow trephine from the iliac crest showed the presence of bone consisting of a few delicate bony trabeculae and a very cellular marrow. There was no evidence of myelosclerosis. The marrow consisted almost entirely of myeloid cells, both mature and immature. The histological features were consistent with myeloid leukaemia.

Peripheral blood taken at the same time as the trephine showed a white cell count of 84,000 per c.mm.

A liver biopsy showed a well marked inflammatory infiltrate, the recognizable cells of which were mature polymorphonuclear leucocytes in the portal tracts as well as small foci of infiltration by polymorphonuclear cells in the liver parenchyma sinusoids, where a few immature cells were seen. The cells, however, were so tightly packed in the portal tracts that it was not possible to exclude the presence of immature forms.

In view of the normal alkaline phosphatase of the white cells and in spite of the bone marrow report, a diagnosis of leukaemoid reaction was made and, as the clinical features fitted in with disseminated tuberculosis, Streptomycin 1.0 g. daily and INH 400 mg. were commenced.

The following day a severe melaena developed, requiring 6 pints of blood, after which the haemoglobin was 15.2 g. %.

In spite of his anti-tuberculous treatment, the patient continued to deteriorate, becoming weaker with accelerated weight loss and a continual Pel-Ebstein type of temperature ranging from 98-101°F. The abdomen increased in size with increasing abdominal tenderness.

At this stage a barium meal demonstrated a large mass displacing the stomach anteriorly and encroaching on the posterior stomach wall and to a lesser extent displacing the stomach medially. The spleen, although enlarged, did not account for the marked displacement of the stomach. The X-ray findings suggested that, in addition to a large spleen, there was a large retroperitoneal mass which was infil-

trating the stomach and was in all probability of the lymphosarcoma group or a tumour of the tail of the pancreas.

The subsequent symptoms were a feeling of increasing fullness of the stomach, intractable abdominal pain and weight loss. There was progressive anaemia without occult blood in the stools, requiring repeated blood transfusions. In spite of therapy death supervened 7 weeks after admission. The white cell count preterminally was 150,000 per c.mm.

SUMMARY OF THE POST-MORTEM FINDINGS

1. Non-differentiated adenocarcinoma of the tail of the pancreas with local infiltration into the stomach and adjacent lymph nodes.
2. Intense leukaemoid reaction without any demonstrable bone metastases.
3. A thrombotic tendency associated with carcinoma of the pancreas, with resultant multiple infarcts in the spleen.

Case 2. A White male aged 66 years presented with pain in the right hypochondrium radiating to the back. This pain was of 3 months' duration. For 2 weeks before his first consultation he had been running a temperature of up to 101°F.

He was an ill, dehydrated male, with a blood pressure of 180/80 mm. Hg. The liver was enlarged downwards 6 finger breadths from the costal margin at the mid-clavicular line. On percussion, liver dullness extended upwards to the 4th interspace. Tenderness was present over the whole liver area. Fluoroscopy revealed good movement of both diaphragms.

A tentative diagnosis of suppurative liver abscess was made and the patient was treated with tetracycline.

A full blood count demonstrated a haemoglobin of 14.3 g. %; packed cell volume, 44%; MCHC, 33%; leucocytes, 16,000 per c.mm., with 78.5% neutrophils, 5% monocytes and 16.5% lymphocytes. The erythrocyte sedimentation rate was 43 mm. in 1 hour (Wintrobe). The platelets were normal in number.

A week later the patient was put on to Chloroquine tablets 1 *t.d.s.*, with some subjective improvement after 6 days, but he was still running a low-grade fever.

A liver biopsy revealed liver tissue infiltrated by large trabeculae of anaplastic carcinoma. The component cells exhibited considerable pleomorphism and mitotic activity. Glandular structures were not present and secreting activity could not be demonstrated. There was no evidence to suggest that this tumour arose in the liver.

A full blood count was repeated. It showed a haemoglobin of 13.2 g. %, a leucocyte count of 56,000 per c.mm. with 84% mature polymorphonuclear cells, 1% eosinophils, 6.5% monocytes and 8.5% lymphocytes.

Prednisone 40 mg. daily was administered. This resulted in a drop of the white cell count from 56,000 to 9,800 per c.mm. 9 days later. Six weeks later it had risen again to 49,000 per c.mm. in spite of continued prednisone.

A few days later the patient died; an autopsy was refused. A possible source of the primary neoplasm was the biliary system, as this patient had had a gall stone for many years.

DISCUSSION

The alkaline phosphatase of the white cells in the first case was of cardinal diagnostic importance in differentiating granulocytic leukaemia from leukaemoid reaction. The following are the relevant factors of the alkaline phosphatase of the white cell in relation to disease.

According to Tanaka *et al.*[4] the white cell alkaline phosphatase is increased in diseases which have as their common denominator increased adrenocortical activity, e.g. pyogenic infection, myocardial infarction, trauma and diabetic acidosis, as well as in polycythaemia vera, the mechanism of the increase in the latter disease being undetermined.

These authors reiterate the fact that there is a decrease of the alkaline phosphatase of the white cells in granulocytic leukaemia.

They also found extremely low levels in all but 1 of 7 cases of paroxysmal nocturnal haemoglobinuria, the one exception being in complete remission.

Low levels were found in most cases of idiopathic thrombocytopaenic purpura, but in this condition, unlike in chronic myeloid leukaemia, the administration of ACTH for 72 hours brought the levels to normal or above.

In glandular fever the alkaline phosphatase seems to be depressed during the acute stage of this disease.

Myeloid metaplasia occurs in a heterogeneous group in which some cases show a low alkaline phosphatase and some are normal.

According to Gingold and Jejtel[5] the alkaline phosphatase may not always help, e.g. in glandular fever, and they suggest that the blood histamine level, which increases many hundreds of times in chronic myeloid leukaemia, may be a useful differentiating test.

CONCLUSIONS

The two cases reported here illustrate leukaemoid reactions in carcinoma. However, tuberculosis, pertussis and glandular fever can

present with a leukaemoid reaction and it is especially important in tuberculosis to arrive at the correct diagnosis because acute disseminated tuberculosis requires urgent anti-tuberculous treatment which may be life-saving.

Forkner[6] quotes cases of tuberculosis causing disease resembling both the acute and chronic types of leukaemia.

SUMMARY

Two cases of leukaemoid reactions in carcinoma are presented.

The differential diagnosis by alkaline phosphatase and blood histamine levels is described.

Our thanks are due to the Acting Medical Superintendent (Dr. J. S. Enslin) of the Johannesburg General Hospital for permission to submit the first case for publication, and to Dr. M. M. Suzman for his constant help and for the case records of the second case.

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AMYLOZINE (TRIFLUOPERAZINE–AMYLOBARBITONE):

A CLINICAL TRIAL IN GENERAL PRACTICE

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May (1961)[5] recently published the results of a controlled clinical trial with this preparation for the treatment of neurotic symptoms in hospital patients. In the past 6 months we have conducted a modified trial on mentally disturbed patients seen in general practice.

Among the oldest and most persistent symptoms from which mankind suffers are worry, tension and depression; and the general practitioner has become increasingly aware of the large numbers of patients reporting for advice and treatment in his busy surgeries. The mechanical prescribing of sedatives and tonics, followed by the inevitable appeal to the overworked psychiatrist, has provoked a situation wherein the general practitioner has been forced into the major role of psychotherapist. May[2] stated that when the stability of the equilibrium between stress and personality is disturbed, there are various effective measures which may serve to re-establish the balance. The first measure (mitigating the stress) seldom succeeds as this may entail major changes in the patient's life over which the practitioner has no adequate control. The second measure (to lower the impact of stress by reduction of awareness) may be achieved by barbiturates, but this often leaves the patients, even in successful cases, in a drowsy and non-alert condition. The third measure (which utilizes drugs like the phenothiazines) reduces emotional reaction to stress by interference with the central activating mechanisms which normally maintain the background of cortical alertness and awareness. Other measures, which involve surgery, cannot be considered by general practitioners.

Psychotherapy may, in many cases, produce efficient and lasting stabilization but the general practitioner, as a rule, is unable to do this and prefers to refer his patients to psychiatrists. This procedure is not always possible, so that it is often necessary for general practitioners to provide symptomatic relief by drugs in order to tide the patients over periods of stress. The results have been encouraging.

In general practice the control of neurotic symptoms is usually readily established by the

use of drugs. Trifluoperazine (Stelazine), which acts at the subcortical levels, has already been shown to give good results in psychoneurotic patients.[2, 3] However, this drug, useful though it has been, has on occasions produced states of excitability more than desired. It was therefore considered that another drug, amylobarbitone, acting at the cortical level, in combination with Stelazine might prove to be a more powerful corrective to neurotic symptoms than either drug used alone. Amylozine, a combination of Stelazine and amylobarbitone, was thus made available for clinical trial for this purpose.

Its effect on psychoneurotic patients in a controlled trial by May[2] was most encouraging. The results of a trial in patients seen in 2 practices form the substance of this paper.

METHODS AND MATERIALS

Amylozine, in Spansule Capsule form, is a long-acting preparation which at first contained 1 mg. of Stelazine and 1 grain of amylobarbitone. It was soon realized that the dose of Stelazine was possibly too low, so this was increased to 2 mg. in later supplies used in the trial. The daily dose was 1 Spansule Capsule taken morning and evening, and it was found that only on rare occasions was it necessary to increase the dose temporarily to 3 Spansule Capsules a day.

The patients chosen for study were unselected in as much as those who were diagnosed as suffering from mental disturbances and needing treatment were included in the trial. A record card was available for each patient; on it were noted the diagnosis and a brief history of the complaint. Almost all patients seen had previously been treated with other preparations so it was also possible, on clinical grounds, to make a comparative assessment of the value of Amylozine in relation to previous therapy. The patients were not encouraged to think that they were being given a new 'miracle' drug and the whole trial was conducted in as restrained a manner as possible. The record cards permitted us to make observations on the special features associated with psychoneurotic diseases. Amongst the symptoms and signs evaluated were appearance, depression, anxiety and tension, apathy, lassitude, ability to concentrate, irritability, sleep, headaches, gastro-intestinal symptoms, capacity to work, and so on.

The patients were treated for a period of 6 weeks, as a rule, and in many cases a follow-up was possible on subsequent occasions. As most of the patients were well known to us, we could reasonably claim that our evaluation of the results of treatment was valid. When patients evidenced complete, or almost complete, remission of symptoms, which was maintained, the results were recorded as *Excellent.*

TABLE 1

Diagnosis	*No. of Patients*	*Results*			
		Excellent	*Good*	*Fair*	*Poor*
Anxiety States	69	8	43	11	7
Menopausal Depression	8	0	4	4	0
Reactive Depression	4	0	2	1	1
Endogenous Depression	2	0	0	1	1
Hysteria	2	0	0	0	2
Puerperal Depression	1	1	0	0	0
Senile Degenerative Condition	5	1	1	1	2
Post-operative Condition	2	1	0	1	0
Premenstrual Tension	2	0	2	0	0
Anxiety States in Congestive Cardiac Failure	2	1	0	0	1
Total	97	12	52	19	14

Good results were regarded as a decided improvement with a partial remission of symptoms. If there was only slight improvement, not sufficient to alter the care and status of the patient, the results were recorded as *Fair*. If the condition remained unchanged, or worsened, these results were recorded as *Poor*.

RESULTS

Table 1 records the results obtained in all the patients treated with both strengths of drug. Table 2 records the results in 19 patients treated with the lower Stelazine dosage preparation. A total of 97 patients was treated. Their ages varied from 20-81 years. Of the 97 patients treated 12 were recorded as *Excellent*, 52 as *Good*, 19 as *Fair*, and 14 as *Poor* results. Thus 64 patients responded satisfactorily to treatment, whereas in 33 the results were considered unsatisfactory. The largest group treated consisted of patients suffering from anxiety states. In these 51 satisfactory and 18 unsatisfactory results were obtained. There were another 28 patients treated in 9 different diagnostic categories.

Table 1 shows that where there was a clear aetiological factor for the illness, results were not as good as in the anxiety state group. In our experience, Amylozine was not particularly satisfactory in reactive, senile or endogenous depressions.

SIDE EFFECTS

Side effects were of little consequence. One patient complained of increased restlessness and tension. A second patient complained of increased depression in association with an urticarial rash. A third patient had bizarre feelings of unreality and dreaminess. Only one patient complained of drowsiness.

Depression was not much relieved in most of the patients, but anxiety and tension were rapidly ameliorated. The ability to concentrate was soon improved and there was a beneficial effect on apathy and lassitude.

DISCUSSION

The results of this trial suggest that Amylozine is a valuable preparation for the treatment of psychoneurotic states where anxiety and tension are the predominant features. The combination of amylobarbitone and Stelazine in a single capsule appeared to be much superior in effect to either of these drugs given alone. In our experience, the almost complete lack of side effects makes the combination a very safe preparation for use in general practice and is a justification for this form of treatment. May[2] stated that each of the components may interfere in a different way with the mechanism which underlies the production of emotional tension, which presumably involves the cortical and subcortical systems. As these 2 systems are interdependent, each exercises an influence on the other which determines the final level of emotional tone. In the anxiety state group the results were most encouraging, but in the other groups not enough patients were treated to enable us to make a satisfactory evaluation.

In the treatment of psychoneurotic patients who are agitated or in whom previous treatment with Stelazine may have produced some restlessness and insomnia, Amylozine should certainly be prescribed, as it not only alleviates the symptoms of this group of diseases but

TABLE 2

Diagnosis	*Results*			
	Excellent	*Good*	*Fair*	*Poor*
Anxiety State	—	11	2	3
Endogenous Depression	—	—	—	1
Menopausal Depression	—	—	1	—
Reactive Depression	—	—	1	—
Total	—	11	4	4

Table 2 shows the results obtained in the 19 patients who were treated with the lower dose of Stelazine in the compound. Of these 11 were satisfactory and 8 unsatisfactory. In the main group, *Anxiety State*, 11 results were satisfactory and 5 were not. Comparing the effect of the higher with the lower Stelazine dosage in the anxiety state group, it is seen that a slightly better response was obtained with the higher amounts of Stelazine.

also allows undisturbed sleep and inhibits restlessness.

SUMMARY

1. Ninety-seven patients suffering from mental disease, of whom 77 were psychoneurotics and 20 psychotics, were treated with Amylozine, a combination of Trifluoperazine (Stelazine) and amylobarbitone.

2. Sixty-four patients responded satisfactorily to treatment, the best results being obtained in the anxiety state group.

3. The side effects due to treatment were negligible.

4. Amylozine can be recommended as a safe therapeutic preparation for use in general practice.

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THE TREATMENT OF NON-EUROPEAN SCHIZOPHRENIC PATIENTS

IN A SPECIAL UNIT WITH MELLERIL

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Numerous publications[1-5] testify to the effectiveness and lack of serious side effects of Melleril (thioridazine) for the treatment of schizophrenic patients. However, none of those publications gives special consideration to the peculiar difficulties encountered in the treatment of non-European psychotics, e.g. difficulties of communication between psychiatrist and patient, overcrowding of mental hospitals for non-Europeans, understaffing, and unreliability as well as illiteracy of nursing staff.[6] Our hospital is faced with these difficulties. For this trial it was therefore decided that the therapy would be carried out in the best available condititons existing in Mathari Hospital, though these fell far short of what was really required. The ward selected was adapted for requirements, and improved living conditions (plenty of bed space, fresh air, adequate toilet facilities, recreational facilities, etc.) were provided. Other wards in the hospital were purloined of various items of equipment. Posters of a topical nature were pasted around the walls of the ward, and these incidentally were not destroyed by the patients. All the various articles expected in a hospital ward were available, such as plenty of linen and clothing, liberal soap, towels and good feeding arrangements. Therapy and nursing were intense and vigorous. A high standard of conduct and hygiene was set, and staff for the Unit were the best available.

The 22 patients selected for the trial were reviewed before commencing therapy. Their physical health was further investigated and improved, if possible, especially regarding anaemia and intestinal parasites.

Staff. African staff (5 in number) selected to work in the Unit were chosen for reasons of dependability, intelligence and a willingness to work. No trained staff were in the Unit, because there were none available. A European male nurse kept a watching brief, gave advice and generally saw that the programme laid down was carried out. No additional staff was required for relief duties for off duty, the Unit being independent from the rest of the hospital. An additional man looked after the Unit as well as another ward during the night time.

The special Unit operated from 1 to 31 March 1960 when, owing to staff shortage, it had to be disbanded. In cases where an improvement in mental health was seen during this month, therapy was continued in other wards. Owing to the very high degree of illiteracy among the staff, a simple chart was designed with questions requiring 'yes' or 'no' for an answer. From this, and from the European male nurse's observations, progress was assessed.

Despite our extremely careful selection of staff, the attitude of Africans in placing themselves first before the patients, seen so often here, again showed itself. Unless a European nurse supervised them closely, the African staff tended to let things slide, and forget the programme.

PROGRAMME

The object of the programme was that every minute of the patients' waking day should be gainfully used. The programme briefly was:

health and hygiene education, occupational therapy, team work and organized games, lectures on current affairs, group discussions (a lot of difficulties were encountered here, but could be overcome), recreational facilities (card games, dominoes, Snakes and Ladders, football), organized rest periods.

Material. Our trial was conducted on 22 male patients with the following diagnoses:
Catatonic schizophrenia: 7.
Schizophrenic illness: 11.
Schizophrenic illness + mental deficiency: 2.
Schizophrenic illness + epilepsy: 1.
Malingering: 1.
The details are shown in Table 1.

TABLE 1

Number	*Diagnosis*	*Previous Therapy*	*Melleril Dose (Per Day)*	*Results*
206/59	Catatonic Schizophrenia	ECT, Chlorpromazine	600 mg.	Greatly improved, discharged to relative.
94/59	Catatonic Schizophrenia	ECT, Chlorpromazine	600—900 mg.	Markedly improved, discharged to relative.
250/59	Catatonic Schizophrenia	ECT, Chlorpromazine	600—800 mg.	'Cured', discharged.
247/59	Catatonic Schizophrenia	ECT, Chlorpromazine (Ataxia)	600–1200 mg.	Unimproved.
256/55	Chronic Schizophrenia	ECT, Chlorpromazine	500—600 mg.	Cured, to be discharged.
44/56	Schizophrenia + Mental Deficiency	ECT, Chlorpromazine Prochlorperazine	600—1200 mg.	Permanently much improved.
161/56	Schizophrenia + Mental Deficiency	ECT, Chlorpromazine	600 mg.	Permanently much improved.
220/56	Schizophrenia	ECT	500—600 mg.	Quieter and more cooperative, otherwise unimproved.
271/56	Schizophrenia	ECT, Chlorpromazine	300—900 mg.	Much improved whilst on Melleril
128/59	Catatonic Schizophrenia	ECT, Chlorpromazine	600—900 mg.	Unimproved.
247/57	Schizophrenia	ECT	600 mg.	Completely recovered, discharged.
182/57	Schizophrenia	ECT, Chlorpromazine	600—900 mg.	Much improved whilst on Melleril.
67/59	Schizophrenia	ECT	600 mg.	Moderately improved.
251/59	Schizophrenia	ECT, Chlorpromazine	300 mg.	Recovered, discharged.
207/59	Schizophrenia + Epilepsy	ECT, Chlorpromazine	300 mg.	Much improved whilst on Melleril; relapsed when discontinued.
82/50	Malingering	ECT, Chlorpromazine	600 mg.	Much improved, gave up malingering, discharged to prison.
197/59	Schizophrenia	ECT	500 mg.	Greatly improved, discharged.
205/58	Schizophrenia	ECT, Chlorpromazine	600 mg.	Unimproved.
154/58	Catatonic Schizophrenia	ECT	500—900 mg.	Much improved, discharged.
232/58	Schizophrenia	ECT	600 mg.	Unimproved.
204/59	Schizophrenia	ECT, Chlorpromazine (Ataxia)	300—600 mg.	Recovered, discharged.
264/59	Schizophrenia	Chlorpromazine	600 mg.	Improved but dull and depressed.

RESULTS

Of the 22 patients in this study 18 improved; one man gained as much as 10 lb. in weight.

Every patient in the group slept soundly each night. Before therapy, in quite a number of cases, night sedation had been necessary.

Not one case of violence was seen. This was remarkable because most of these patients had a history of violence in other wards.

One schizophrenic mental-defective, who usually refused to wear clothes, started to wear his clothes, go to the toilet and could be gainfully occupied, while he remained in the Unit.

A criminal lunatic, who was malingering, decided to act normally.

The epileptic patient had 3 *grand mal* seizures whilst in the Unit; it was noted that there was no confusion or violence after the fits.

Six patients were discharged home as recovered; 3 patients recovered sufficiently to be discharged from the hospital into the care of relatives; 8 patients were not discharged from the hospital but were improved (some only whilst they received Melleril, with relapses soon after discontinuing medication); 4 patients were not improved. The patient who had been malingering is not included in these figures. Under Melleril treatment he gave up his malingering and was transferred to prison. Up to 9 February 1961 none of the 9 patients, discharged between April and July 1960, had relapsed.

SIDE EFFECTS

Seventeen cases of marked drowsiness were observed on the first day, due to overdosage. (We initially started on a dosage of 200 mg. 3 times daily). This was overcome by reducing the initial dosage to 100 mg. 3 times daily and building up to 300-1200 mg. per day over a period of 14 days. One case of vomiting occurred on the first day; this also disappeared when initial dosage was reduced and then built up.

CONCLUSION

A Psychiatric Unit working on the lines we have outlined had a good measure of success. We had here the worst possible patients, makeshift equipment, inexperienced staff and inadequate facilities, yet reasonable results were obtained.

It is strongly urged that before Units are opened experienced staff, equipment and conditions are made available, that competent persons be consulted and their advice sought.

It is considered that Melleril enabled the patients to respond to the improved environment provided in the special ward, and it was the combination of the two which gave the satisfactory results. It is not thought either would be adequately satisfactory on its own.

ILLUSTRATIVE CASE REPORTS

1. *Case No.* 250/59 (*Male, Aged* 23 *Years, Kakamega Tribe*). On 30 October 1959, he was certified by a medical practitioner as being of unsound mind, as he was talking irrelevantly and he was very noisy and troublesome.

When he was admitted to Mathari Hospital on 11 December 1959, he was depressed, pre-occupied, conversing with hallucinatory voices and stated that he saw people who were trying to beat him, because they wanted to steal his maize, beans and oil. He had noisy outbursts of behaviour, when he attacked others. He was reported to be rather dangerous.

He had 8 ECT's from 12 December 1959 to 11 January 1960. This resulted in marked improvement.

However, on 14 January he was reported to be restless and dirty, chlorpromazine was commenced (150 mg. *t.i.d.*). By 11 February 1960 he was having 250 mg. *t.i.d.* without any improvement, so on 18 February this was discontinued, as he was rather weak and feeling the effects of the high dosage.

He commenced Melleril on 1 March 1960, 200 mg. *t.i.d.* On 10 March this was increased to 800 mg. daily and on 18 March he was reported to be much better, but admitted to hearing hallucinatory voices. On 28 March he said that he no longer heard the voices, but remembered when he did. Melleril was continued until 12 May 1960, when the patient was reported to be rather slow and quiet, but otherwise normal.

He was discharged from hospital on 15 July 1960 as quite normal.

The diagnosis was catatonic schizophrenia.

2. *Case No.* 204/59 (*Male, Aged* 15 *Years, Kikuyu Tribe*). He was first certified on 9 October 1959, as he was listening to imaginary voices, he was noisy, restless and disorientated.

He was admitted to Nairobi Prison on 15 September 1959 and he commenced ECT treatment. By 13 October 1959 he had had 8 ECT's without a satisfactory response.

He commenced chlorpromazine on 13 October 1959, which he had in doses of 100 mg. *t.i.d.*, but this was discontinued 2 days later, after he had been knocked unconscious by another patient.

He was admitted to Mathari Hospital on 16 November 1959. ECT was commenced on 18 December 1959. He had had a total of 22 treatments on 20 January 1960, without any improvement.

On 22 January 1960, he recommenced chlorpromazine and had 100 mg. *t.i.d.*, but this was discontinued on 18 February. He was not really improved and did not seem to be tolerating the chlorpromazine very well. He was rather uncertain on his feet.

He commenced Melleril on 1 March 1960, 100 mg. *t.i.d.* By the end of March he was slightly improved and on 28 April the Melleril was increased to 200 mg. *t.i.d.* By 9 June 1960 he was considered to be normal. He was attending the hospital school and he was cooperative and cheerful.

On 16 June 1960 the Melleril was discontinued and he was discharged on 1 July 1960 as recovered.

The diagnosis was schizophrenic illness.

3. *Case No.* 247/57 (*Male, Aged* 54 *Years, Maragoli Tribe*). He was first certified by a medical officer as being mentally sick on 28 August 1952.

The certificate stated he was rambling and incoherent, with delusions, and he was responsible for dangerous attacks on other members of his location.

He was admitted to Mathari Hospital on 3 September 1952, when he was suffering from auditory hallucinations, was very asocial and had outbursts of noisy behaviour.

He was given 10 ECT's, made a fair recovery and was discharged on 31 October 1952.

He was re-admitted on 9 April 1954, when he was noisy, restless and creating a lot of trouble. He had 3 more ECT's, settled fairly quickly and was discharged on 26 May 1954.

He was again re-admitted on 7 September 1956. He had 24 further ECT's and on 30 January 1957 he had shown some improvement. He was fit for discharge on 3 June 1957.

He was re-admitted on 2 December 1957, when he was talking and shouting continuously in response to auditory hallucinations, and there were periods of restless, noisy behaviour. He had a further 15 ECT's; this did not result in any real improvement.

On 1 March 1960, Melleril was commenced 200 mg. *t.i.d.* and at the end of the month, even though still very deluded, he would converse a little.

Melleril was continued up to 23 June 1960, with a slow but very astounding improvement. On that date Melleril was discontinued and he was apparently quite normal.

He was discharged from this hospital on 1 July 1960, apparently completely recovered.

The diagnosis was schizophrenic illness.

4. *Case No.* 161/56 (*Male, Aged* 24 *Years, Benjun Tribe*). On 26 April 1956 he was certified as being insane on the following grounds: that he did not understand or attempt to reply to simple questions and he was dirty in his habits and played with his faeces. He was sometimes very violent, breaking doors and windows, had tried to throw children over the sea wall and had tried to rape his own mother on several occasions.

He was admitted to Mathari Hospital on 15 June 1956, when he refused to give a correct answer to any questions. He replied with the first thought that came into his head, e.g.: 'I have been here 2 days,' or 'I live over there.'

He gave the impression of being mentally retarded.

He did not show any interest in his surroundings, in the ward he was dull, apathetic, continually rubbing his fingers together.

He commenced ECT and on 1 October 1956, after he had had 16 treatments, there was no improvement.

On 13 June 1959 he commenced chlorpromazine; doses up to 75 mg. *t.i.d.* did not effect any improvement. Chlorpromazine was discontinued on 23 July 1959.

Melleril was commenced on 1 March 1960. He had 200 mg. *t.i.d* On 10 March he had shown some definite improvement and the opinion was definitely formed that there was a marked degree of mental deficiency present. On 28 March 1960 he was so much improved that he was able to take an interest in rope making in the Occupational Therapy Department. On 28 April 1960 the Melleril was discontinued. His improvement seems to have been maintained.

The diagnosis in this case seems to be mental deficiency with schizophrenic illness.

SUMMARY

A group of 22 non-European psychotic patients (schizophrenics) were subjected to a trial which combined administration of a new phenothiazine, Melleril, together with improved nursing and ward conditions.

Eighteen of the 22 patients improved; 9 could be discharged from hospital. None of them has relapsed within the 7-9 months since their discharge.

We acknowledge the free trial supplies of Melleril made available to us by Sandoz Limited, Basle.

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METHOHEXITAL

A CLINICAL TRIAL OF A NEW OXYGEN BARBITURATE

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The barbiturate 1-methyl-5-(1-methyl-2-pentynyl)-5-allyl-barbituric acid has the structural formula shown in Fig. 1.

Two of its carbon atoms (marked with an asterisk in Fig. 1) act as centres of asymmetry and therefore there exist 4 stereoisomers known respectively as the αl, βl, αd and βd forms. The original compound investigated was a mixture of all 4 forms and was known as Compound 22451. This proved unsatisfac-

tory due to a high incidence of stimulation, tremors and twitching, leading in isolated cases to generalized convulsions. The 4 stereoisomers were then investigated independently by Gibson *et al.*

A racemic mixture of the high melting point isomers αd and αl was known as Compound 25398. This has since received the name of methohexital. It will be seen that this barbiturate contains an oxygen atom in place of the sulphur atom of the thiobarbiturate group and is thus more closely related to quinalbarbitone and pentobarbitone than to thiopentone.

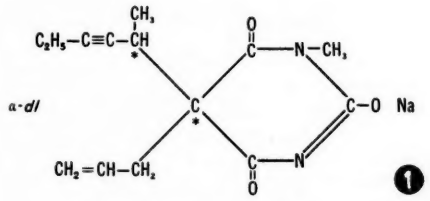

Fig. 1. The Structural Formula.

The sodium sulphate is readily soluble in water or saline to yield a clear solution of pH 10–11. It is stable in aqueous solution for 6 months at 25°C., and for one year at 5°C.

PRESENT STUDY

Methohexital sodium was given in a 1% solution in sterile saline by intermittent intravenous injection. The series consists of 68 consecutive unselected cases. It was followed by a series of 500 consecutive unselected cases which received intermittent injections of 2.5% thiopentone sodium solution for anaesthesia to provide a control series for the incidence of hiccup only. Speed of injection was varied in an attempt to regulate the incidence of hiccups, but no significant differences could be found clinically or statistically, so that this aspect is not dealt with further.

The total series consists of 68 cases which are analysed in Tables 1–4.

TABLE 1

Sex

Male	18
Female	50
Total	68

TABLE 2

Age (In Years)

Under 2	0
2–9	0
10–19	6
20–29	5
30–39	13
40–49	14
50–59	11
60–69	8
70+	11
Total	68

TABLE 3

Preoperative Condition

Good	56
Fair	10
Poor	2
Total	68

TABLE 4

Nature of Operation

Cystoscopy and pyelogram	17
Dilatation and curettage	14
Colporrophy	5
Appendectomy	3
Abdominal hysterectomy	3
Insertion of radium	3
Vaginal hysterectomy	2
Trendelenburg and stripping of varicose veins	2
Laparotomy	2
Prostatectomy	1
Cholecystectomy	1
Gastrectomy	1
Pyloroplasty	1
Total colectomy	1
Subtotal thyroidectomy	1
Perirenal air insufflation	1
Removal F.B. of foot	1
Ranulectomy	1
Haemorrhoidectomy	1
Halsted operation	1
Vulvectomy	1
Inguinal herniorraphy	1
Progesterone implant	1
Circumcision	1
Sigmoidoscopy	1
Dilatation parotid duct and sialogram	1
Total	68

TECHNIQUE OF ANAESTHESIA

The present series was divided into 2 subseries as follows:

Subseries A: 37 *Cases.* These received only methohexital supplemented by nitrous oxide 6

L/min. and oxygen 2 L/min. from a Boyle's machine, i.e. the partial pressure of nitrous oxide varied between 470 and 520 mm. Hg at the altitude at which the series was carried out. The semiclosed system was used (Mapleson A). No relaxants, assisted or controlled respiration was used.

Subseries B: 30 *Cases*. These were patients induced with methohexital and then maintained with nitrous oxide and oxygen plus either ether or halothane with or without relaxants and controlled respiration. Varying techniques of anaesthesia were used. The results are analysed separately.

It will be noted that one case has been excluded. This was done as it fitted into neither group, being a methohexital induction followed by maintenance with intermittent methohexital and relaxants using controlled ventilation with carbon dioxide absorption. This case showed no complications and was unremarkable in every respect.

Premedication. Premedication was according to weight, age and the condition of patient and given intramuscularly ¾–1 hour preoperatively (Table 5).

TABLE 5

Atropine only	19
Meperidine and atropine	47
Omnopon and scopolamine	1
Promethazine and atropine	1
Total	68

STATISTICAL ANALYSIS OF SUBSERIES A

Highest total dosage = 740 mg.
Lowest total dosage = 160 mg.
Median total dosage = 300 mg.
Mean total dosage = 335 mg.
Standard deviation = ±105 mg.
Longest duration of anaesthesia = 65 minutes.
Shortest duration of anaesthesia = 5 minutes.
Median duration of anaesthesia = 14 minutes.
Mean duration of anaesthesia = 16 minutes.
Highest dosage rate = 52 mg. per minute.
Lowest dosage rate = 9.0 mg. per minute.
Median dosage rate = 20.0 mg. per minute.
Mean dosage rate = 26.0 mg. per minute.
Standard deviation = ±12.6 mg. per minute.

STATISTICAL ANALYSIS OF SUBSERIES B

Highest total induction dose = 320 mg.
Lowest total induction dose = 140 mg.
Median total induction dose = 200 mg.
Mean total induction dose = 204 mg.
Standard deviation = ±43 mg.

RESULTS

TABLE 6

Complications	26	=	38%.
No complications	42	=	62%.
Total	68	=	100%.

TABLE 7

Hiccups	21	=	31%.
Coughing	3	=	4%.
Laryngeal spasm	2	=	3%.
Bronchospasm	1	=	1%.
Vomiting	1	=	1%.
Apnoea	1	=	1%.

TABLE 8

Premedication	*Hiccups*	*No Hiccups*	*Totals*
Atropine ..	9	10	19
All other premedications ..	12	37	49
Totals	21	47	68

$\chi^2 = 4.059$ $p = < .05$ (i.e. the probabilities are that this result may occur by chance in one case out of 20 trials).

TABLE 9

Barbiturate	*Hiccup*	*No Hiccup*	*Totals*
Thiopentone ..	2	498	500
Methohexital ..	21	47	68
Total	23	545	568

$\chi^2 = 135.3$ $p = < .001$ (i.e. the probabilities that this result may occur by chance are once in a 1,000 trials).

From Tables 6 and 7 it will be seen that hiccups were the most frequent complication. These followed immediately on induction, being well pronounced and regular and usually commented upon unfavourably by the surgeon. Hiccups were not abolished by giving more methohexital. They continued for from 1–10 minutes, but usually nearer the latter figure. Hiccups seldom returned after the administration of a single dose of 40–50 mg. of succinylcholine to facilitate endotracheal intubation. The clinical impression that the incidence of hiccups was much more in patients not receiving sedative premedication is confirmed by Table 8, which indicates significance at the 5% level.

Table 9 illustrates the quasi-certitude that methohexital is a much more potent cause of hiccups than thiopentone.

The incidence of tremors was not specifically recorded but our impression was that these were not prominent or alarming in this series, probably because of the larger and more rapid dosage than in other published series. Where

methohexital was given slowly and in low dosage early in the series, minor tremors were noticed.

Apnoea was not a prominent feature in spite of the relatively high dosage. One case showed a 2-minute apnoea following 200 mg. of methohexital.

One case showed coughing, laryngospasm and bronchospasm which are all 3 tested separately in Table 7 and account for half the respiratory complications (excluding apnoea and hiccup). This patient was judged a very poor risk and had severe emphysema and bronchospasm before anaesthesia and cardiac decompensation with a gallop rhythm. It was felt that methohexital was not solely implicated in the complications which ensued.

On the whole cough, laryngeal spasm, apnoea and vomiting were not prominent and the clinical impression was that the incidence of these complications was of the order of that obtained with thiopentone.

Only one patient complained of pain along the vein immediately following injection in comparison with the high (60%) incidence noted by Taylor and Stoelting[4] with Compound 22451.

There were no cases of post-operative thrombophlebitis. No deaths occurred in this series up to 2 weeks after anaesthesia.

DISCUSSION

1. *Hiccup.* This was the most interesting feature noted in this series due to its very high frequency of occurrence, viz. 31%. Friedman,[2] who gave a standard dosage of 165 mg. with atropine and succinylcholine for electroconvulsive therapy, makes no mention at all of this complication.

Taylor and Stoelting[4] noted hiccup in 85 of 3,340 (2.5%), Wynant *et al.*[5] in 3 out of 10 cases, Weyl *et al.*[7] in 4 out of 200 (2%). Redish *et al.*,[10] although providing a space headed 'hiccough' in their record card, make no mention of the incidence observed.

Several authors state that adequate premedication lowers the incidence of complications and especially that of hiccup. With this conclusion we are in entire agreement (Table 8). No special effort was made to treat the hiccups when they occurred.

In one series the particularly low incidence may be accounted for by the frequent preoperative administration of intravenous barbiturates and alpha-prodine in the theatre before anaesthesia.

We did not notice that the administration of more methohexital abolished the hiccups and indeed we are inclined to believe that our relatively high dosage of methohexital may have been a causative factor in the high incidence of hiccups observed. Hiccups did disappear following deepening of anaesthesia with other agents, but it also disappeared when no effort was made to deepen anaesthesia. We feel that other authors may have fallen into the error of *post hoc propter hoc* reasoning in this respect.

Samuels[9] believes that the combined action of respiratory and phrenic centres together with the hypothalamic sympathetic centres may actually perform the work of a specific hiccup centre. Case records of neurosyphilis, head injury, cerebro-vascular accident, brain tumour, etc. developing hiccups, strengthen this view.

We know that Compound 22451 has a stimulant and convulsant action on some part of the brain and that this is also true to a lesser extent of methohexital. It is tempting to postulate a direct chemical action on a 'hiccup centre.' Methohexital and related compounds may prove important tools in the experimental production and study of hiccups. Much has been written on the treatment of intractable hiccups, particularly on the continent, but a thorough search of the literature of the subject reveals very little more on the aetiology and pathogenesis to us than it did to Samuels[9] in 1952.

We are of the opinion that this complication is the most important single feature making routine use of methohexital undesirable in the rather high dosage we have employed.

Dosage. It will be noted from the results quoted for subseries B that the mean induction dose was 200 mg. with a S.D. of ±43 mg. This is considerably higher than that used by other workers averaging 70 mg.,[4] 165 mg.,[2] 5.02 mg. per minute,[3] 54.4 mg.;[6] for most patients 51–100 mg.,[7] 134 mg.[10] On the other hand, we must mention that our average induction dosage of thiopentone is roughly 400 mg. ±100 mg., which is more than most anaesthetists would use. Wyant *et al.*[5] used methohexital in 7 subjects at a dosage of 273 mg. per sq. meter of body surface, which is higher than our dosage. They state that this dosage is 7½ times the average induction dose and that their patients recovered within 20 minutes. We found that the higher dosage reduced considerably the incidence of body tremors and made for a much smoother induction. This higher dosage may, however, account for our high incidence of hiccups (31%) compared with other series.

Waking Times. The major claim made in favour of methohexital by those who support its use is that it shortens the waking time when compared with the thiobarbiturates.

Redish *et al.*,[10] in their recent comparative statistic study of the agents thiopentone,

methohexital and methitural, determined 3 points called the 'Awake time,' the 'Romberg time' and the 'Leave time.' These are respectively the times which elapsed between the end of anaesthesia and:

1. The time when patient could state his own name correctly;
2. The time when the Romberg sign would no longer be elicited;
3. The time when the patient was judged fit to leave by competent observers.

No statistically valid correlation could be found between the respective times for thiopentone and methohexital, although there was a difference significant at the 5% level between methohexital and the thiopentone and methitural groups combined. Part of one of their Tables is reproduced here (Table 10) to illustrate that, whatever the statistical evidence may be, the actual variations of average times obtained cannot be regarded as of any practical advantage.

TABLE 10

	'Awake' Time	*'Romberg' Time*	*'Leave' Time*
Methohexital	5.1 minutes	26.8 minutes	37.2 minutes
Methitural	7.9 minutes	34.2 minutes	44.3 minutes
Thiopentone	5.2 minutes	34.4 minutes	42.1 minutes

Egbert *et al.*[8] tested 14 patients anaesthetized with methohexital during the recovery phase with a complex reaction timer obtained from the Automobile Association of America. Their data show that the duration of effect of methohexital is only two thirds as long as that of thiopentone, but they noted that early ambulation was associated with the occurrence of hypotension and suggested that caution should be employed in this respect.

Heaton,[3] using the Bender face-hand test, could find no statistically significant differences in the recovery times from methohexital and thiopentone. The actual average waking times were 22.2 minutes and 24.4 minutes respectively.

Taylor and Stoelting,[4] with a series of 3,340 patients, have only a clinical impression to support their conclusion that methohexital showed shorter duration and more consistently rapid awakening and termination of anaesthesia than other barbiturates.

Gibson *et al.*[11] believe that the short action is in part due to a faster breakdown in the liver than in the case of thiopentone, where 10–15% of drug present in the body is broken down by the liver per hour. This factor may be important after prolonged intermittent dosage with relatively large amounts, but it is well known that the rapid recovery from the so-called short-acting intravenous barbiturates, is due to redistribution in the body with consequent rapid fall in the effective blood level.

In the use of methohexital this factor still appears of paramount importance. A critical examination of the literature on methohexital does not show any practical advantage to be obtained from its use in short anaesthesias. In contrast, the subconvulsant nature of the drug and the occurrence of hiccups appear to be strong disadvantages.

SUMMARY AND CONCLUSIONS

1. A series of 68 cases anaesthetized with methohexital is described.

2. Methohexital was given in higher dosage than in previous series.

3. A very high incidence of hiccups (31%) was found at this high dosage level.

4. Adequate premedication lowered the incidence of but did not abolish hiccups.

5. A critical survey of the literature on methohexital was made and in our opinion this showed no evidence of any practical advantage in rapidity of recovery as compared with thiopentone.

ADDENDUM

Since the preparation of this paper our attention has been drawn to a further paper by Wynant and Barr.[12] These authors found in a 'blind' study of 56 thiopental and 55 methohexital anaesthetics, that a highly significant difference in waking times was attained. The difference in the mean waking time was 4.7 minutes (15–10.3 minutes). Interestingly enough, no hiccups were noted in any of these 111 cases.

We should like to express our appreciation and thanks to the Eli Lilly Research Laboratories, Indianapolis, Indiana, U.S.A., for their generous supply of methohexital.

This investigation was sponsored by the Council for Scientific and Industrial Research.

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THE HYDRATION SCALE

A USEFUL DIAGNOSTIC INSTRUMENT IN PRIVATE PRACTICE

S. LEVIN, M.B. (RAND), M.R.C.P. (EDIN.), D.C.H.
Johannesburg

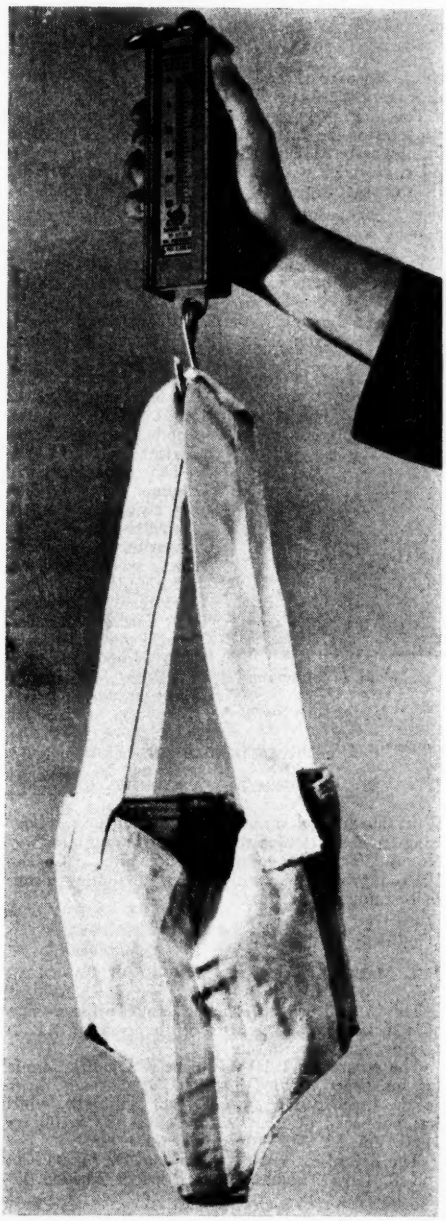
'Oh that my grief were thoroughly weighed, and my calamity laid in the balances together.'
Job, 6:2.

When one is first presented with a sick baby, impressions of the state of hydration are purely clinical; but in following the course of dehydration there is no better method than serial weighing. When one is confronted with a baby who has begun to vomit or to pass loose stools, the thermometer, stethoscope, throat spatula and otoscope are of little value; it is far more important to record the weight. With such a point of reference established, repeated observation and repeated weighing can markedly facilitate clinical management, especially in instances of hypertonic dehydration, when clinical evidence of dehydration may not be apparent, though repeated use of the scale will reveal its development.

An ordinary spring scale is adequate. These are cheap, handy, and weigh up to 25 lb. within an accuracy of half a pound. This is all that is necessary during the first year of life, when problems of hydration are most frequent and most urgent. Greater accuracy of recording is not required, and even if the spring eventually stretches so that the true weights are a pound or two out, this is of no consequence, for all subsequent weighings are based on the same standard. In any event some of the spring scales have an adjustment screw for correcting any inaccuracy of weighing, should this occur.

A home-made canvas hammock suspended from the hook of the scale completes the instrument (Fig. 1).

It takes but a few moments to weigh an infant and if, over the course of a day or two, there is significant weight loss, i.e. largely fluid loss, then the scale will furnish strong indications for parenteral fluid replacement.



NOTES AND NEWS : BERIGTE

Dr. Teddy Schneider recently left Johannesburg for a visit to Germany, the United Kingdom and the U.S.A. He will attend the International Diabetic Congress in Geneva and the Israeli Medical Congress to be held from 14–25 August 1961 in Jerusalem.

Dr. Schneider is accompanied by his wife. They will return to Johannesburg before the end of August.

* * *

Mr. I. Norwich (Part-Time Head of the Department of Surgery, Edenvale Hospital), is presenting a paper *A Ten-Year Survey of Stabs in the Abdomen*, at the Congress of the International Society of Surgeons in Dublin early in September 1961.

Dr. Norwich will be accompanied by his wife on his overseas trip.

* * *

DR. M. L. SIMENHOFF: ELI LILLY MEDICAL RESEARCH FELLOW (SOUTH AFRICA) FOR 1961

Dr. M. L. Simenhoff, of Cape Town, and who is at present doing research work at the British Postgraduate Medical School, Hammersmith, has been appointed the Eli Lilly Medical Research Fellow (South Africa) for 1961.

Dr. M. L. Simenhoff

Dr. Simenhoff will assume the tenure of his award at Harvard University, in the Department of Medicine, where he will work under Prof. John P. Merrill, Director of the Cardio-Renal Section, Peter Bent Brigham Hospital, Boston 15, Mass., U.S.A.

* * *

PHYSICAL MEDICINE

WONDERFUL OPPORTUNITY

Will any medical man who is interested in specializing in Physical Medicine please communicate with No. A. Y. X., c/o Medical Proceedings, P.O. Box 1010, Johannesburg, with a view to joining a very well-established practice.

* * *

THE MAURICE WEINBREN AWARD IN RADIOLOGY

This Award (which is made annually for a paper of sufficient merit) consists of the sum of R50.00 together with a certificate.

The Award for 1959 was made to Dr. Eric Samuel for his paper entitled *The Use of Contrast Media in the Investigation of the Acute Abdomen*, which was published in *The British Journal of Radiology*, 1960, Vol. 33, No. 386, pp. 82–91.

The Award for 1960 was made to Drs. Josse Kave and R. Glyn Thomas for their paper entitled *The Problem of Abnormal Radiological Lung Patterns*, which was published in *Medical Proceedings*, 1960, Vol. 6, No. 15, pp. 323–332.

S. F. Oosthuizen (*Chairman*).
H. A. Shapiro (*Honorary Secretary*).

P.O. Box 1010, Johannesburg.

* * *

ELECTION OF DR. GEORGE GORDON CAMPBELL TO HONORARY FELLOWSHIP OF THE ROYAL SOCIETY OF SOUTH AFRICA

Para. 1 of Chapter III of the *Statutes* of the Royal Society of South Africa makes provision for two classes of Fellows, Ordinary and Honorary. While under the Charter the number of Ordinary Fellows may not exceed 100, the *Statutes* place no finite limit on the number of Honorary Fellows but state:

'The list of Honorary Fellows shall be strictly limited. They shall be elected from those who have done distinguished and outstanding work in the furtherance of Science in South Africa.'

Once every 2 years the Council is entitled to recommend to the Society for election not more than 2 persons who have either rendered conspicuous service to the cause of Science in South Africa or are such that their election would be of signal service or benefit to the Society.

This right the Council rarely exercises but, after full consideration the Council resolved this year to recommend to the Society for election to Honorary Fellowship Dr. George Campbell of Durban, in recognition of the manifold services that he and his family have rendered over many years to Science in South Africa.

CITATION

PREPARED BY A MEMBER OF THE COUNCIL

'Dr. George Campbell has been Chairman for many years of the Councils of both the Natal Technical College and the University of Natal and, by his great vitality and personal influence amongst the people of Natal, he has contributed greatly to the unprecedented development of these two institutions in the post-war years. He played a prominent role in the establishment of the Faculty of Medicine at the University of Natal. In these activities he has continued a family tradition: his father Dr. Sam Campbell was largely responsible for initiating and establishing the Natal Technical College in Durban and played some part in the founding of the Natal University College.

Dr. G. G. Campbell

Dr. Campbell is, and has been since its foundation, the President of the South African Association for Marine Biological Research. It is largely due to his energy, enthusiasm and initiative that the South

African Association for Marine Biological Research was founded and brought to its present flourishing condition. He played a major part in raising the funds and obtaining the support that led to the building of the very fine aquarium at Durban that attracts so much attention and admiration to-day. He has recently succeeded in securing further financial support that will enable the Association to proceed with the erection of research laboratories and a shark canal.

He is a medical practitioner, not a professional scientist, but I do not know anybody who has done more for the cause of science in South Africa than he has. He and his family, in fact, have done a very great deal for education in Durban which has not, in my opinion, received the recognition it deserves.'

* * *

UNIVERSITY OF NATAL

JUNE 1961 MEDICAL GRADUANDS

The following candidates have completed the requirements for the M.B., Ch.B. Degrees of the University of Natal:

	Ramiah, Y.
Mestry, P.	Reddy, F. S.
Ntsepe, J. W. R.	Vandayar, D. K.

THE NUTRITION SOCIETY

ADVANCE NOTICE OF 145TH MEETING

The following is the programme of a symposium to be held at the National Institute for Research in Dairying, Shinfield, Reading on Friday, 13 October 1961 on:

Agricultural Problems in Underdeveloped Countries.

Chairman: Professor R. G. Baskett, *O.B.E.* (Director, The National Institute for Research in Dairying).

Professor L. Dudley Stamp, *O.B.E.* (London School of Economics): *Limitations of Climate and Soil.*

Dr. Audrey I. Richards (Newnham College, Cambridge): *Human Problems Concerned in Increasing Agricultural Production.*

Mr. T. J. Lansbury (University College of Ghana): *Livestock Production with Particular Reference to the Nutritional Problems of West Africa.*

Dr. C. F. Hickling, *C.M.G.* (Colonial Office, London): *Fish Production in Underdeveloped Countries.*

Prof. A. H. Bunting (University of Reading): *Problems of Increasing Arable Production.*

D. F. Hollingsworth,
(*Honorary Programmes Secretary*).

Ministry of Agriculture, Fisheries and Food,
Great Westminster House,
Horseferry Road,
London, S.W.1, England.

PREPARATIONS AND APPLIANCES

CORTENSOR

A NEW CARDIAC TONIC

Westdene Products (Pty.) Ltd. announce the introduction of **Cortensor,** the new cardiac preparation from the research laboratories of Dr. A. Wander of Switzerland.

Cortensor, the simple aliphatic amine-6-amino-2 methyl heptanol-(2) (called briefly heptaminol) is primarily a sympathomimetic agent, whose digitalis-like cardiotonic effects considerably outweigh its peripheral vasoconstrictive and central analeptic action. Its most important well balanced effects are:

Intensification of the systolic contraction comparable to that produced by strophanthin G as regards promptness of onset, intensity and duration.

Improvement of cardiac blood flow similar to that of current theophylline preparations.

Resuscitation of the heart muscle, without risk of promoting extra-systoles or cardiac fibrillation.

Control of arterial hypertension, while blood pressure and pulse rate remain within normal limits.

Intensification of diuresis and only slight stimulation of nervous centres.

These advantages place **Cortensor** between the highly active cardiac glycosides and other adrenergics with more powerful vasoconstrictive and central analeptic effects.

The range of dose from the threshold of activity to the production of noticeable side effects (tachycardia, palpitations, etc.) is so wide that dosage can be prescribed without any risks for both prematures and infants and for senile patients.

The therapeutic response to **Cortensor** lasts for only a few hours and has the advantage of not being cumulative and therefore permitting extremely accurate dosage.

It must be stressed that in severe cases of cardiovascular insufficiency, **Cortensor** does not replace the more powerful drugs. Nevertheless, **Cortensor** provides a means of sparing these drugs for emergency cases, of increasing its effectiveness when combined with these drugs, of frequently reducing their dosage and thus improving their tolerability or of replacing them when they cause pronounced side effects.

Cortensor is supplied in bottles of 12 and 20 tablets, in Drops (15 c.c.) and in injection form (5 c.c.).

Further information may be obtained from the sole South African Distributors:

Westdene Products (Pty.) Ltd., P.O. Box 7710, Johannesburg.

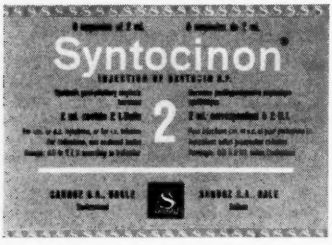
SYNTOCINON 2 I.U. IN 2 ML.

Sandoz announce the introduction of ampoules of **Syntocinon** (synthetic oxytocin) containing 2 I.U. of oxytocin B.P. in 2 ml.

Syntocinon is the pure, synthetically manufactured oxytocic principle of the posterior pituitary and thus it is absolutely free of vasopressin and other foreign polypeptides. **Syntocinon** is used essentially as an oxytocic for induction of labour and in intra-partum

and post-partum uterine inertia; as well as in breast engorgement for its 'milk let-down effect'.

The new strength and size of **Syntocinon** ampoules of 2 I.U. in 2 ml. allows for more exact dosage of small quantities, particularly where **Syntocinon** is used for



intermittent intramuscular administration of small doses. The 2-Unit ampoule is also very suitable for use in cases of incomplete abortion and in cases of breast engorgement. Moreover, the **Syntocinon** 2 I.U. ampoule will render useful services where smaller amounts than 5 I.U. are given in an intravenous drip, e.g. if Theobald's method of giving 0.5 I.U. in 500 ml. is being applied.

How Supplied: Boxes of 6 ampoules x 2 ml.

For samples and literature, please write to:

Sandoz Pharmaceutical Department, P.O. Box 4461, Johannesburg.

AMYLOZINE SPANSULE CAPSULES

Composition: Trifluoperazine 2 mg. Amylobarbitone 64·8 mg. (gr. 1).

Description: A preparation specifically developed for the treatment of agitation, apprehension and insomnia, **Amylozine** combines the highly efficient tranquillizing properties of trifluoperazine with the sedative action of amylobarbitone.

Each component complements the other to provide a therapeutic action ideally suited for the symptomatic treatment of the chronic agitated pshychoneurotic or acutely apprehensive patient.

The onset of effect of **Amylozine** is prompt and, because the preparation is presented as a **Spansule** sustained-release capsule, is maintained for 12 hours with a single dose.

Indications: Treatment of chronic, agitated psychoneurotics and acutely apprehensive patients, whose state of mind is marked by insomnia, fatigue, vacillation, moodiness and fear.

Contra-Indications and Cautions: Idiosyncrasy to barbiturates. Use cautiously in patients with cardiac or hepatic impairment.

Side Effects: Those associated with either component, e.g. dry mouth, dizziness, blurred vision, lassitude or transient drowsiness may occasionally occur, but in the dosage recommended are minimal and infrequent.

Dosage: For adults and children over 12 years—one **Amylozine** Spansule capsule morning and night as required, but not to exceed 3 capsules daily.

Presentation: **Spansule** capsules in containers of 30.

Further information may be obtained from:

SKF Laboratories (Pty.) Ltd., P.O. Box 38, Isando.

BOOK REVIEW

The Ultrastructure of Cells. By Marcel Bessis. Sandoz Monographs.
Basle: Sandoz Ltd.

The application of the electron microscope in biological work and the perfection of the ultra-microtome have caused radical changes in our concept of the ultrastructure of cells. We fully agree with the author of this monograph that 'we are entering a fascinating world leading from the whole cell to the perfectly defined arrangement of the molecules of which it is built'. To date, knowledge of this 'fascinating world' has been limited to specialists in this new field of investigation. This monograph, written by one of the most eminent cytologists, will undoubtedly serve to introduce a wider audience to the great variety of intracellular structures revealed by the electron microscope.

The author first gives a brief description of the techniques used for the preparation of tissues for electron microscopical investigations and then presents details of the ultrastructure of some of the intracellular organelles, e.g. mitochondria, endoplasmic reticulum, the cell membrane, the nucleus, centrosomes and Golgi bodies, etc. The rest of the monograph is almost entirely devoted to the special fields of interest of the author, i.e. the cytology of the blood and blood-forming organs and the cancer cell. This last part of the book is very specialized; a whole chapter is devoted to a description of the digestion of red blood cells. It would perhaps have been preferable to have given more details of intracellular structure which would be of interest to all cytologists. For instance, no mention is made of desmosomes and lysosomes.

It is gratifying to note that throughout the monograph the author always attempts to correlate the structure and the function of the intracellular organelles. The rapid advances which are being made in this field are exemplified by the fact that in this monograph, printed in December 1960, Bessis regards the manner in which cells secrete substances accumulated in the ergastoplasmic sacs, as an unsolved problem. Since that time Palade of the Rockefeller Institute, New York, has given a complete description of the genesis and secretion of one of these substances, i.e. the zymogen granules of the exocrine cells of the pancreas.

The monograph is lavishly illustrated with numerous electron micrographs, which are of a uniformly excellent quality. The value of the book is considerably enhanced by a relatively complete bibliography which includes some of the European literature so easily overlooked by investigators in this field.

This monograph can be recommended without hesitation to all workers interested in cytology and especially to histopathologists who should become more aware of the potentialities of the electron microscope for the study of the ultrastructure of pathological cells.